PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : G01R 33/54 — A1

(11) International Publication Number: **WO 99/63355**

(43) International Publication Date: 9 December 1999 (09.12.99)

(21) International Application Number: PCT/US99/12443

(22) International Filing Date: 4 June 1999 (04.06.99)

(30) Priority Data:
09/090,166 4 June 1998 (04.06.98) US

(71) Applicant *(for all designated States except US)*: THE GOVERNMENT OF THE UNITED STATES OF AMERICA, represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; Office of Technology Transfer, National Institute of Health, Suite 325, 6011 Executive Boulevard, Rockville, MD 20852 (US).

(72) Inventors; and

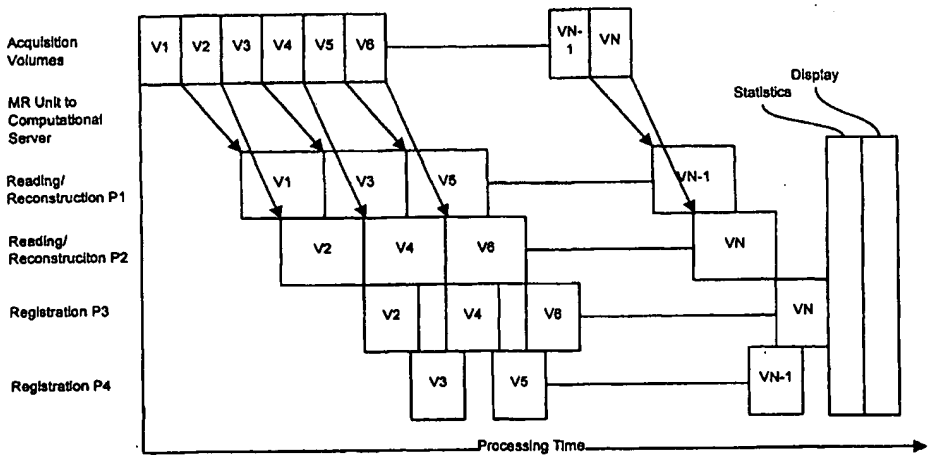
(75) Inventors/Applicants *(for US only)*: FRANK, Joseph, A. [US/US]; 11819 Rosalinda Drive, Rockville, MD 20854 (US). OSTUNI, John [US/US]; Apartment 31, 13001 Crookston Lane, Rockville, MD 20851 (US). DUYN, Jozef [NL/US]; 3900 Decater Avenue, Kensington, MD 20895 (US).

(74) Agent: SCHNELLER, John, W.; Venable, P.O. Box 34385, Washington, DC 20043-9998 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: REAL-TIME INTERACTIVE FUNCTIONAL MAGNETIC RESONANCE IMAGING



(57) Abstract

Raw image data is acquired as it is being produced by a magnetic resonance unit during a functional magnetic resonance imaging (fMRI) examination. Reconstruction, registration, and statistical analysis of the acquired raw image data are performed, and the results are displayed immediately after completion of the acquisition of the raw image data. A parallel processing technique is used to achieve the real-time interactive fMRI.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

REAL-TIME INTERACTIVE FUNCTIONAL MAGNETIC RESONANCE IMAGING

FIELD OF THE INVENTION

The invention relates generally to the real-time display of images for interactive functional magnetic resonance imaging (fMRI).

REFERENCES

For the convenience of the reader, the publications referred to in the specification are listed below. In the specification, the numerals within parentheses refer to the respective publications. The listed publications are incorporated herein by reference.

(1) Sorensen AG, Tievsky AL, Ostergaard L, Weisskoff RM, Rosen BR. Contrast agents in functional MR imaging. J Magn Reson Imaging 1997;7;47-55.

(2) Bruening R, Kwong KK, Vevea MJ, et al. Echo-planar MR determination of relative cerebral blood volume in human brain tumors: T1 versus T2 weighting, AJNR. Am J Neuroradiol 1996;17:831-40.

(3) Bruening R, Wu RH, Yousry TA, et al. Regional relative blood volume MR maps of meningiomas before and after partial embolization. JCAT 1998;22:104-110.

(4) Baird AE, Benfield A, Schlaug G, Siewert B, Lovbald KO, Edelman RR, Warach, S. Enlargement of human cerebral ischemic lesion volumes measured by diffusion weighted. Magnetic Resonance Imaging Ann Neurol 1997;41:581-589.

(5) Tsuchida C, Yamada H, Maeda M, et al. Evaluation of peri-infarcted hypoperfusion with T1* weighted dynamic MRI. JMRI 1997;7:518-522.

(6) Aronen HJ, Glass J, Pardo FS, et al. Echo-planar MR cerebral blood volume mapping of gliomas. Clinical utility. Acta Radiol 1995;36:520-8.

(7) Mattay VS, Duyn JH, Kotral KJ, et al. Brain Mapping using Functional MRI: A Direct comparison between dynamic contrast and "BOLD" methods. Radiology 1995;194:687-693.

(8) Petrella JR, DeCarli C, Dagli M, et al. Assessment of Whole Brain Vasodilatory Capacity with Acetazolamide Challenge at 1.5T using Dynamic Contrast Imaging with FS-Burst. Am J Neuroradiol 1997; 18: 1153-1161.

(9) Petrella JR, DeCarli C, Dagli M, et al. Age related vasodilatory response to acetazolamide challenge in healthy adult humans: A dynamic contrast-enhanced MR perfusion imaging study. Amer J Neuroradiology 1998;19:39-44.

(10) Duyn JH, Yang Y, Frank JA, Mattay VS, Hou L. Functional magnetic resonance neuroimaging: data acquisition techniques. Neuroimage 1996;4: S76-S83.

(11) Duyn JH, van Gelderen P, Barker P, Frank JA, Mattay V.S, Moonen CTW. 3D Bolus Tracking with Frequency-Shifted BURST MRI. JCAT 1994; 18: 680-687.

(12) Williams DS, Detre JA, Leigh JS, Koretsky AP. Magnetic resonance imaging of perfusion using spin inversion of arterial water. Proc Natl Acad Sci U S A 1992; 89(1):212-6.

(13) Ye FQ, Smith AM, Yang Y, et al. Quantitation of regional cerebral blood flow increases during motor activation: A steady- state arterial spin tagging study. Neuroimage 1997;6:104-12.

(14) Ye FQ, Pekar JJ, Jezzard P, Duyn J, Frank JA, McLaughlin AC. Perfusion imaging of the human brain at 1.5 Tesla using a single shot ept spin tagging approach. Magn Reson in Med 1996;36:219-224.

(15) Yang Y, Frank JA, Hou L, Ye F, McLaughlin A, Duyn JH. Multislice imaging of cerebral perfusion with pulsed arterial spin-tagging, MRM in press 1998.

(16) Kim SG, Tsekos NV. Perfusion imaging by a flo-sensitive alternating inversion recovery (FAIR) technique: Application to functional brain imaging 1997;37:425-435.

(17) Mattay VS, Frank JA, Santha AKS, et al. Whole Brain Functional Mapping with Isotropic MR imaging. Radiology 1996;201:399-404.

(18) Yang Y, Glover GH, Frank JA, et al. A comparison of Fast MR scan Techniques for cerebral Activation Studies at 1.5 Tesla. Mag Reson in Med 1998;39:61-67.

(19) Bandettini PA, Jesmanowicz A, Wong EC, Hyde JS. Processing strategies for time course data sets in funtional MRI of the human brain. Mag Res Med 1993;30:161-173.

(20) Mueller WM, Yetkin FZ, Hammeke TA, et al. Functional magnetic resonance imaging mapping of the motor cortex in patients with cerebral tumors. Neurosurgery 1996;39:515-20.

(21) Cox RW, Jesmanowicz A, Hyde JS. Real-time functional magnetic resonance imaging. Magn Reson Med 1995;33:230-6.

(22) Yang Y, Glover GH, van Gelderen P, et al. Fast 3D Functional Magnetic Resonance Imaging at 1.5 T with Spiral Acquisition. Magn Reson Med. 1996;36:620-626.

(23) Atlas SW, Howard RS 2d, Maldjian J, et al. Functional magnetic resonance imaging of regional brain activity in patients with intracerebral gliomas: findings and implications for clinical management. Neurosurgery 196;38:329-38.

(24) Duyn JH, Yang Y. Single shot spiral functional MRI with trapezoidal gradients. J Mag Reson 1997;128:130-134.

(25) Cosgrove GR, Buchbinder BR, Jiang H. Functional Magnetic Resonance imaging for intracranial navigation. Neurosurgery Clinics of North America 1996;7:313-322.

(26) Kerr AB, Pauly JM, Hu BS, et al. Real-time interactive MRI on a Conventional Scanner. Mag Res Med 1997;38:355-367.

(27) Jackson JI, Meyer CH, Nishimura DG, Macovski A. "Selection of a convolution function for Fourier inversion using gridding." IEEE Trans. Med. Imaging 1991;10; 473-478.

(28) Ostuni J, Levin R, Frank JA, DeCarli C. Correspondance of Closest Edge Voxels- A robust registration algorithm. J Mag Reson Imaging 1997;7:410-415.

(29) Ostergaard L, Weisskoff RM, Chesler DA, Gyldensted C, Rosen BR. High resolution measurement of cerebral blood flow using intravascular tracer bolus passages. Part I: Mathematical approach and statistical analysis. Magn Reson Med 1996;36:715-25.

(30) Ostergaard L, Sorensen AG, Kwong KK, Weisskoff RM, Gyldensted C, Rosen BR. High resolution measurement of cerebral blood flow using intravascular tracer bolus passages. Part II: Experimental comparison and preliminary results. Magn Reson Med 1996;36:726-36.

(31) Alsop DC, Detre JA. Reduced transit-time sensitivity in noninvasive magnetic resonance imaging of human cerebral blood flow. J Cereb Blood Flow Metab 1996;16:1236-49.

(32) Ostuni, JL, Santha, AKS, Mattay, VS, Weinberger, DR, Levin, RL, Frank, JA, Analysis of interpolation effects in the reslicing of functional MR images JCAT 1997;21:803-810.

(33) MEDx [tm], Version 2.2, Sensor Systems, Reston Virgina.

(34) Cox RW. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput Biomed Res 1996;29:162-73.

(35) Hacklander T, Reichenbach JR, Weule J, Modder U. An efficient and robust PC program to calculate MR based regional cerebral blood volume maps. Computerized Medical Imaging and Graphics 1997;21:51-62.

(36) Hesser J, Manner R, Braus DF, Ende G, Henn FA. Real-time direct volume rendering in functional magnetic resonance imaging. MAGMA 1997;5:87-91.

(37) Duyn JH, Frank JA, and Moonen CTW. Incorporation of Lactate Measurement in Multi-Spin-Echo Proton Spectroscopic Imaging. Magn. Res. Med. 1995; 33: 101-107.

(38) Buckner RL, Bandettini PA, O'Craven KM, et al. Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging. Proc Natl Acad Sci U S A 1996; 93:14878-83.

(39) Moriarty TM, Kikinis R, Jolez FA, Black P. McL, Alexander III E. Magnetic Resonance Imaging Therapy. Neurosurgery Clinics of North America 1996;7:323-331.

(40) Pearlman JD and Edelman RR. Ultrafast Magnetic Resonance Imaging Segmented turboflash, echo-plananr and real time nuclear magnetic resonance. Radiological Clinics of North America 1994;32:593-612.

(41) Leung DA, Debatin JF, Wildermuth S, et al. Real-Time biplanar needle tracking for interventional MR imaging procedures. Radiology 1995;197:485-588.

(42) Kasner SE, Grotta JC. Emergency identification and treatment of Acute Ischemic Stroke. Ann Emergency Medicine 1997;30: 642-653.

(43) Albers GW. Rationale for early intervention in acute stroke. Am J Cardiol 1997;80:4D-10D.

BACKGROUND OF THE INVENTION

fMRI facilitates the study of dynamic physiologic processes by measuring the changes in magnetic resonance (MR) signal intensity during rapidly acquired serial images. fMRI studies, for example, can be used to determine the following: 1) relative cerebral blood volume (rCBV) and relative cerebral blood flow (rCBF) using dynamic contrast enhanced MRI (1-11); 2) absolute cerebral blood flow (CBF) using spin tagging techniques (12-16); and 3) localized increases of neuronal activity in response to neurophysiological

stimulation using blood oxygenation level dependent (BOLD) contrast (17-25). By using rapid scanning techniques, such as single shot echo planar imaging (EPI) or spiral imaging, each fMRI study usually acquires large raw data sets, which are comprised of hundreds or thousands of images, in relatively short periods of time (18, 24, 25).

These fMRI data sets are conventionally not reconstructed on the MR unit because reconstruction would interfere with or delay the start of subsequent fMRI experiments. Instead, the raw data is conventionally stored and subsequently transferred to an off-line workstation for analysis, which usually occurs long after the subject has left the MR unit (21-25).

Typically, analysis of fMRI data sets usually take several hours to days (21, 25) before they are reviewed because of the delays in off-line reconstruction, registration, and subsequent statistical analysis of the raw image data. Time is also required to archive all unprocessed raw image data files and images. Although the most important part of this computational process lies in the ultimate analysis of the fMRI images, for which various software packages are available (33, 34, 35, 36), the bulk of the initial time commitment is spent on the reconstruction, registration, and storage of the images. As a result of this conventional process, even a quick review of activation maps usually occurs long after the subject has left the MR scanner. Due to delays imposed by the MR unit, researchers have tended to limit the number of experimental trials acquired during a one-hour scanning session, in part because the researchers are unsure of the reliability and integrity of their studies.

Moreover, the fMRI results are often inadequate due to motion artifacts or poor compliance because of inadequate understanding of the paradigm. To obtain adequate fMRI results when an initial fMRI exam has gone awry, the subject needs to reschedule another fMRI exam, return to the fMRI facility, undergo the additional fMRI exam, await the results of the additional fMRI exam, and possibly reschedule yet another fMRI exam if the results are again poor. Because of the significant costs of MRI exam time, the increased backlog of MRI exams, and the increased discomfort and displeasure of the subject, this conventional approach of repetitive studies is unsatisfactory for both the researcher and the subject.

Real-time fMRI approaches have been proposed previously. For example, Cox et al. (21) proposed an algorithm that recursively computes the correlation coefficient of an

image sequence with a reference vector and simultaneously removes any undesired linear trend from the data. Activation maps were displayed using a predetermined statistical threshold. This process was performed at various time points during a BOLD EPI study acquired at a single location while the subject performed a finger tapping experiment. The authors indicated that their algorithm was not a complete substitute for post-processing, where multiple statistical tests can be applied to the raw data sets for detection of the activation and suppression of the artifacts. However, the authors indicated that the benefit of their approach is to look primarily for spuriously correlated artifacts.

With the approach of Cox et al. (21), the temptation exists to truncate an experiment early because the statistical maps generated appear to give the results that the investigators required. This temptation should be avoided. A decision to halt a study early could result in an arbitrary number of epochs collected, which would confound any type of intra-subject or inter-subject comparisons. Moreover, any interim analysis of an fMRI study as a consequence of a real-time display should impose a more stringent (higher) threshold level for significance to define activation.

As another example of prior art attempts, real-time reconstruction and display of MR data have been used successfully to direct single slice MR fluoroscopic based imaging techniques to localize anatomical structures of guide and monitor intervention procedures (25, 39-41). Further, Kerr et al. (26) demonstrated the utility of a real time interactive MRI on a conventional scanner with abdominal and cardiac imaging.

SUMMARY OF THE INVENTION

With the invention, an fMRI examiner can immediately evaluate the results from an fMRI examination of a subject while the subject is still in the MR unit. If the results are poor, the examination can be performed again without the need or expense of having to reschedule the subject for another fMRI examination. Further, if the results dictate performing additional fMRI examinations, these examinations can be immediately performed without the need or expense of having to reschedule the subject for another fMRI examination.

For example, with the invention, results of a whole brain BOLD activation experiment with isotropic voxels (17, 18, 24) could guide the planning of a subsequent perfusion experiment (i.e., dynamic contrast enhancement or spin tagging). These types of

studies, all performed within a single fMRI exam session, allow the examiner to review the BOLD activation map and then to either vary the work load of the task or repeat the study multiple times to observe changes associated with reproducibility, learning, or precision.

The advantages of real-time interactive fMRI include: 1) examining the data for artifacts that may contaminate the images (i.e., physiological motion); 2) developing or modifying activation paradigms quickly, allowing the examiner to test an hypothesis while the subject is still in the MR unit; and 3) developing new paradigms on-line, and thereby making fMRI a more flexible neurological tool. Furthermore, the immediate display of the analyzed results of BOLD, perfusion (i.e., spin tagging) or dynamic contrast fMRI studies also allows for the evaluation of the subject to a provocative pharmacological challenge (e.g., the Wada or sodium ambitol test). Real time analysis of an fMRI exam also permits a direct comparison to the baseline condition of the subject, and may provide valuable information relating to neurological integrity and functional status of the subject. With interactive fMRI, sequential fMRI exams can be designed in which, for example, the results of an initial BOLD activation study guides other functional (i.e., spin tagging, dynamic contrast) or metabolic imaging (37) examinations to a specific area of interest or to repeat the paradigm with changes, such as higher spatial and/or temporal resolution (38).

Interactive fMRI can also be useful to dynamic contrast studies. In particular, dynamic contrast enhanced fMRI studies are usually performed once during an imaging session and are being used as part of an early evaluation of an acute ischemic event or an evaluation of central nervous system (CNS) pathology (1,6). These results may be useful in monitoring the treatment effects of antithrombolytic agents in an acute stroke (4), and have been shown to be useful in grading primary central nervous system (CNS) malignancies (16). With the invention, analysis of the calculated rCBV, rCBF, and time-to-peak (TTP) maps after completion of the acquisition of the raw image data may provide further insight into the efficacy of novel therapies.

The success of an interactive fMRI based physiological interview depends on the investigator being able to: 1) review processed and statistically analyzed image maps shortly after the completion of the fMRI acquisition; 2) determine if the study needs to be repeated; or 3) if a modification is required to the paradigm, further elucidate cerebral response. This sequence of events should occur while the subject is in the MR unit in order to take advantage of the experimental conditions. With the invention, the

neuroscientist is provided with an analysis of large fMRI data sets within seconds after completion of the MR acquisition.

The invention, in its preferred embodiment, costs less than most major MRI hardware upgrades, while simultaneously providing researchers with a more efficient use of MR scanner time, and ultimately increasing the number of clinical and research studies performed.

Moreover, the invention facilitates the on-line planning and evaluation of various protocols (e.g., spectroscopic imaging, dynamic contrast CBV, arrival time maps, and perfusion CBF measurements. The invention can be used in conjunction with other modalities to study the effect of carotid stenosis on cerebral perfusion (11), or become part of a work-up for a brain attack (1, 5, 42, 43). Further, the invention can be used for adaptive task tuning (e.g., increasing the stress-load) or repeating unsuccessful scans (e.g., subject motion) used for brain mapping (12, 18), or pre-surgical planning of eloquent cortex relationship to a surgical target (3, 25, 23, 44), and other therapeutic interventions, as will become apparent to one of ordinary skill in the art. Moreover, the invention can be used to integrate fMRI techniques into clinical practice, and as a valuable tool for improving the care of patients with neurological and psychiatric disorders.

It is an object of the invention to provide a parallel processor hardware system, along with post-processing techniques, to display statistical results of an fMRI exam co-registered on anatomic images and to allow for the rapid evaluation and preliminary interpretation of the fMRI exam.

It is another object of the invention to provide a hardware and software configuration using parallel processors that cost less than most MR hardware upgrades and that rapidly performs the following tasks: 1) performs MR acquisition by capturing the raw image data on-the-fly; 2) reconstructs the image files; 3) registers all volumes; 4) performs a predefined statistical analysis for either a BOLD fMRI study or a dynamic contrast study; and 5) displays relevant maps within seconds after the completion of the MR acquisition.

The above objects and advantages are achieved by the invention, which includes a method, an apparatus, and an article of manufacture for the real-time display of the results from an interactive fMRI examination.

In particular, the invention includes a method for outputting results from a magnetic resonance image examination. The method comprises: obtaining first and second acquisition volumes from a magnetic resonance image scanner during the magnetic resonance image examination; processing the acquisition volumes from the magnetic resonance image scanner to obtain the examination results; and outputting the examination results. The processing of the acquisition volumes comprises: reconstructing the first acquisition volume using a first processor to obtain a first reconstructed volume; reconstructing the second acquisition volume using a second processor to obtain a second reconstructed volume; and registering the second reconstructed volume using a third processor.

Alternatively, in the method of the invention, the processing of the acquisition volumes comprises: reconstructing the first acquisition volume using a first processor to obtain a first reconstructed volume; reconstructing the second acquisition volume using the first processor to obtain a second reconstructed volume; and registering the second reconstructed volume using a second processor.

Further, the invention includes an apparatus for processing data from a magnetic resonance image examination. The apparatus comprises: a magnetic resonance image scanner for producing a plurality of acquisition volumes obtained during the magnetic resonance image examination; at least one first processor for reconstructing the plurality of acquisition volumes to obtain a plurality of reconstructed volumes; and at least one second processor for registering the plurality of reconstructed volumes to obtain a plurality of registered volumes. The apparatus further comprises: means for processing the plurality of registered volumes to obtain statistical information; and means for outputting the statistical information.

Moreover, the invention includes an article of manufacture as a computer-readable medium embodying code segments for a magnetic resonance image examination. The code segments comprise: code segments for controlling the magnetic resonance image examination to obtain a plurality of acquisition volumes; code segments for controlling at least one first processor to reconstruct the plurality of acquisition volumes to obtain a plurality of reconstructed volumes; and code segments for controlling at least one second processor to register the plurality of reconstructed volumes to obtain a plurality of registered volumes.

The apparatus of the invention includes a computer programmed with software to operate the computer in accordance with the invention. Examples of "computer" include: a general purpose computer; an interactive television; a hybrid combination of a general purpose computer and an interactive television; and any apparatus comprising a processor, memory, the capability to receive input, and the capability to generate output.

The article of manufacture of the invention comprises a computer-readable medium embodying code segments to control a computer to perform the invention. Examples of a "computer-readable medium" include: a magnetic hard disk; a floppy disk; an optical disk, such as a CD-ROM or one using the DVD standard; a magnetic tape; a memory chip; a carrier wave used to carry computer-readable electronic data, such as those used in transmitting and receiving electronic mail or in accessing a network, such as the Internet or a local area network ("LAN"); and any storage device used for storing data accessible by a computer. Further, examples of "code segments" include: software; instructions; computer programs; or any means for controlling a computer.

BRIEF DESCRIPTION OF THE DRAWINGS

The file of the patent contains at least one drawing executed in color. Copies of this patent with the color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Embodiments of the invention are explained in greater detail by way of the drawings.

Figure 1 illustrates a schematic of the hardware configuration of the invention.

Figure 2 illustrates a flowchart of the software configuration of the invention.

Figure 3 illustrates the processing configuration of real-time interactive fMRI using four processors.

Figure 4. illustrates the processing configuration of real-time interactive fMRI using two processors.

Figure 5A shows plots for normalized standard error histograms of all vexed signal intensities for three BOLD fMRI experiments using the invention.

Figure 5B shows plots for the degree of rotation detected and corrected using COCGV for the three BOLD fMRI experiments of Figure 5A.

Figure 6 shows images produced by the invention within 20 seconds after completion of a BOLD fMRI exam.

Figure 7 shows images produced by the invention with 49 seconds after completion of a dynamic contrast fMRI exam.

DETAILED DESCRIPTION OF THE INVENTION

The invention is described in terms of the hardware configuration, the software configuration, the processing configuration, an example, and the results from using the invention.

Hardware Configuration

A preferred embodiment of the hardware configuration is illustrated schematically in Figure 1. A clinical 1.5 Tesla Echo Speed MR unit 1 (General Electric, Milwaukee, WI) is equipped with fast gradient hardware and a 2 gigabyte (GB) magnetic disk drive. A Bit3 VME bus adapter card 2 (Bit3 Computer Corporation, Minneapolis, MN) was added to the MR unit 1 to enable access to the raw image data stored in the bulk access memory (BAM) 3. An S-Bus Bit3 board 4 was also installed on a SPARC 20 Clone 5 (Axil Computer Inc., Concord, MA) and connected to the Bit3 card 2 on the MR unit 1. The SPARC 20 Clone 5 is connected to a computational server 6 using a 10 Base T connection 7. The Bit3 connections facilitated rapid transfer of raw image data sets from the MR unit 1 to the computational server 6 via the SPARC 20 Clone. The computational server 6 includes a four-processor DEC Alpha 4100 (Digital Equipment Corporation, Maynard, MA). In particular, the computational server is equipped with four 433 MHz computer processing units (CPUs), 1 GB of shared random access memory (RAM), and a 16 GB magnetic disk drive.

The SPARC 20 Clone 5 plays two major roles. First, to synchronize the data input and output, the clone 5 serves as a data buffer between the MR unit 1 and the computational server 6. Second, the clone 5 performs byte-swapping of the data from the scanner in the MR unit 1. The second role is necessary due to the incompatibility in the representation of the data between the scanner and the computational server. Further, with additional hardware (e.g., additional SPARC 20 Clones and Bit3 cards), multiple MR units can be connected to the computational server 6, which will allow for time-sharing of the hardware configuration.

The hardware configuration of the preferred embodiment is not a unique solution because it is designed to interface with a specific MR unit hardware and its output. As one of ordinary skill will recognize, analogous computer hardware configurations can be utilized with alternative clinical scanners.

Software Configuration

In Figure 2, a flowchart illustrates the method carried out by the software of the invention. In block 8, raw image data is acquired by the MR unit 1. The user interface preferably allows for the selection of the type of MR pulse sequence used (e.g., EPI or spiral imaging), the type of study being performed (e.g., BOLD dynamic contrast, spin tagging), number of volumes acquired, the matrix size, the paradigm definition, and the statistical thresholds.

In block 9, the raw image data from the MR unit 1 is transferred to the RAM of the computational server 6 using appropriate software for transferring data. Moreover, the software preferably accepts raw image files directly from the MR unit 1 or from storage on the hard disk, tape, or other computer-readable medium.

In block 10, the images are reconstructed by interpolating single-shot spiral data sets on to an orthogonal equidistant grid (27), followed by a two-dimensional Fast Fourier Transformation (2DFFT). The interpolation consists of a regridding algorithm with a Gaussian convolution window.

In block 11, the images are registered using a high speed optimized version of the correspondence of closest gradient voxels (COCGV) registration algorithm (28). This algorithm aligns areas of high intensity change based upon a rigid body transformation of the data sets. Of note, this particular regridding procedure allows for reconstruction of data collected with arbitrary k-space trajectories, including the trajectories characteristic of spiral scanning and EPI (24).

In block 12, statistical analysis of the images is performed. For BOLD fMRI studies, a normalization of the signal intensities across the volumes (VN) is performed. All volumes are normalized so that the mean intensity value of their relevant voxels is identical, which allows for comparison between studies. A baseline correction (BC) is applied on a voxel-by-voxel basis for all voxels within the subject using a third order

polynomial fit over the time series data (17). The "activation" statistical map is determined using an arbitrary user defined threshold for a student t-test.

In block 13, the results of the fMRI exam are displayed for review by the investigator. All activation maps and graphs are displayed on a local video monitor in the MR operator control room, or a hard copy is available using an interface to a color deskjet printer (Hewlett Packard, Palo Alto, CA). In addition, the results can be saved to a computer-readable medium or transferred over a network.

Voxels determined to be statistically significant are superimposed in red onto the initial reconstructed fMRI spiral volume and displayed automatically. An s-map is also displayed and is defined as the standard error of the difference between the scan signal intensity on a voxel-by-voxel basis for all volumes in each epoch (i.e., on and rest conditions) in a box-car paradigm. Further, a histogram of the normalized standard error of all voxel signal intensity over time is plotted and displayed. The normalized standard error is the standard error of the difference between the two means (on vs. off) condition at each voxel divided by the mean signal intensity for these voxels (17, 18).

Other types of information can also be determined and displayed using the invention. For example, for dynamic contrast studies, maps of rCBV, rCBF, and TTP are calculated by fitting a gamma variate function to the signal intensity time-course (1, 7, 8, 9, 11, 29, 30). The fitting is performed for the voxels (50,000 to 150,000) within the subject. The TTP map is obtained by an algorithm searching for the occurrence of the maximum change in signal intensity over time, on a voxel-by-voxel basis. The arterial input function is obtained by searching all voxels within the subject for the greatest signal intensity change and then selecting the voxels with the earliest TTP signal change (8). The average gamma variate fit for the voxels meeting these two criteria was then used for the arterial input function. The deconvolution is based on singular value decomposition (29, 30). The rCBV, rCBF, and TTP maps are then displayed for review by the investigator.

As another example, CBF images acquired by either arterial spin tagging (AST) or a multislice flow-sensitive alternating inversion recovery (FAIR) are processed in a similar manner to the BOLD fMRI studies (12-16, 31). For these studies, a T1 map is crated during a separate acquisition, and these images are registered to the fMRI study. As with the BOLD fMRI studies, the percent change in CBF can be determined by taking the difference between the activation and rest states in response to a neurophysiological

stimulus. The CBF images and the T1 map are then displayed for review by the investigator.

As will be apparent to one of ordinary skill, various other software routines can be implemented to accomplish the functions illustrated in Figure 2.

Processing Software Configuration

Figure 3 illustrates a four parallel processor implementation of the invention using the hardware and software configurations described above. The software for the parallel processors was written in C++ with a TCL/TK interface or graphical interface. The scanner of the MR unit 1 acquires N volumes of raw image data, numbered V1, V2, V3, ..., VN in Figure 3. The first acquired volume V1 is transferred to the first processor P1 of the computational server 6. The first processor P1 reads and reconstructs the first volume V1, which is then used as the baseline volume for the registration of the remaining N-1 acquisition volumes to correct for motion during the scan.

The second acquired volume V2 is transferred to the second processor P2 of the computational server 6. The second processor P2 reads and reconstructs the second volume V2, and passes the reconstructed volume V2 to the third processor P3 of the computational server 6. The third processor P3 registers the reconstructed volume V2 against the reconstructed volume V1.

The third acquired volume V3 is transferred to the first processor P1 of the computational server 6. The first processor P1 reads and reconstructs the third volume V3, and passes the reconstructed volume V3 to the fourth processor P4 of the computational server 6. The fourth processor P4 registers the reconstructed volume V3 against the reconstructed volume V1.

The fourth acquired volume V4 is transferred to the second processor P2 of the computational server 6. The second processor P2 reads and reconstructs the fourth volume V4, and passes the reconstructed volume V4 to the third processor P3 of the computational server 6. The third processor P3 registers the reconstructed volume V4 against the reconstructed volume V1.

The above process continues for reading, reconstructing, and registering all N acquisition volumes. If N is an even integer, processor P1 reads and reconstructs acquired volume VN-1, and processor 2 reads and reconstructs acquired volume V_N. If N is an odd

integer, processor P2 reads and reconstructs acquired volume V_{N-1}, and processor P1 reads and reconstructs acquired volume V_N.

After all the N acquisition volumes have been read, reconstructed, and registered by the four processors P1-P4, the statistics of the fMRI examination are analyzed by the computational server. If one statistical analysis is to be performed, this statistical analysis can be performed by one or more of the processors. Moreover, if a plurality of statistical analyses are to be preformed, these statistical analyses can be performed by a combination of the processors.

Finally, the resulting images, maps, and plots are displayed. The processors of the computational server are utilized as necessary to produce the displayable results.

As one of ordinary skill will recognize, the paradigm illustrated in Figure 3 can be extended to any number of processors. For example, in Figure 4, the invention is illustrated using two processors. As another example, the paradigm can be used with 2*N processors, where N is the number of volumes acquired by the MR unit. For this example, each of the first N processors reads and reconstructs one of the N acquired volumes, and each of the second N processors registers one of the N reconstructed volumes.

As will be apparent to one of ordinary skill, the invention can be implemented using any number of processors and a wide variety of MR techniques. For example, the paradigm can be used with BOLD fMRI, dynamic contrast fMRI, the profusion imaging MRI technique, and cardiac MRI. Moreover, the invention can be used to combine diffusion imaging with fMRI data, or to combine spectroscopic imaging with fMRI data.

Further, as will be apparent to one of ordinary skill, the invention is scalable as faster MR acquisition techniques become available and as larger data files are created. For example, in phased array acquisition, the raw image data generated by the multiple receivers of the phase array can be processed using multiple processors according to the invention. For instance, if four receivers are used, each of the data streams from each of the four receivers can be processed using four processors, as illustrated in Figure 3, and a total of 16 processors can be used to process all four of the data streams from the phased array.

Moreover, the invention can be used as a stand alone post-processing unit. Additionally, the invention can be used with other compatible software packages for a more extensive statistical analysis of the fMRI data set.

Example

Using the invention, a BOLD fMRI exam and dynamic contrast study were performed on the brain of a subject. In order to allow for the highest image acquisition rate within the MR scanner's gradient hardware constraints, a multislice single shot spiral scan acquisition technique was used for all fMRI modalities. Using the maximum gradient slew-rate of 120 T/m/s along with the maximum gradient amplitude of 22 mT m^{-1}, the minimal acquisition window was 22 ms (18, 24) for a 64 x 64 matrix size and a 240 mm field of view (FOV), and the maximum MR scanner acquisition rate was 30 slices/second. Under the same conditions, the duration of the acquisition window for EPI scans was 35 milliseconds. For both the BOLD fMRI studies and the dynamic contrast studies, multislice single shot gradient echo spiral images were obtained. The whole brain was covered in 2 seconds per volume with a nominal in-plane resolution = 3.75x3.75 mm^2, TE=35 ms, TR=55.6 ms, number of slices = 36, slice thickness = 4 mm, and flip angle = 84_. The total acquisition time for the BOLD fMRI study was 4.13 minutes, and the total acquisition time for the dynamic contrast study was 2.67 minutes. Finger tapping activation paradigms (17) were used to evaluate the system performance. For the dynamic contrast studies, Gadopentetate Dimeglumine (Magnevist, Berlex Laboratories, Cedar Knolls, NJ) at 0.1 to 0.2 millimole/kg was injected at 10 cc/sec using an MRI compatible mechanical injector (Spectris, Medrad, Inc., Pittsburgh, PA). To obtain baseline images, there was a scan delay of approximately 15-20 seconds prior to the injection. All clinical studies were performed under an approved Intramural Review Board Protocol at the National Institutes of Health.

Results

For the BOLD fMRI study, Table 1 summarizes the performance characteristics of the invention illustrated in Figure 3 of dividing the various tasks over four processors. Approximately 4 minutes and 8 seconds are required to acquire all 124 raw data volumes used for the BOLD fMRI study. During the acquisition time, the system processes the raw image files with essentially no delay. All 124 volumes are reconstructed and registered, and the statistical analysis is performed and displayed with a running time of 4 minutes and

28 seconds. Hence, with the invention, the information was displayed to the investigator 20 seconds after the fMRI examination was completed.

TABLE 1
Performance Characteristics of System Configuration for BOLD fMRI Examination

36 slice volume acquisition time:	2.0 sec/vol
Raw data volume size:	792000 bytes
DEC read volumes (processors 1, 2):	0.5 sec/vol
Reconstruction (processors 1, 2):	1.5 sec/vol
Registration (processors 3, 4):	1.5 sec/vol
VN, BC, and statistics (processors 1, 4):	10 sec.
Display t-maps with images:	7 sec.
a) Total fMRI acquisition (124 volumes):	4 min. 8 sec.
b) Total processing time with BOLD fMRI data acquisition:	4 min. 28 sec.
Processing time (b-a) after MR data collection ends:	20 seconds*
c) Total processing time with BOLD fMRI data acquisition using a single DEC processor:	15 min. 38 sec.
Time ratio (c/b):	3.5

*includes delay time for the first volume to be completely acquired and transferred over the VME bus.

The invention provides the ability to produce and display immediately the activation t-map, s-map, and normalized standard error histogram 20 seconds after the completion of the MR data acquisition. Further, the BOLD fMRI study results are reliable and reproducible, and are consistent with activation maps obtained with conventional processing strategies, which take hours of processing time (21, 25).

The total processing time reported in Table 1 must be compared to the several minutes of "down-time" usually experienced when performing fMRI studies. This delay is either due to waiting for the array processor to finish reconstructing the images or for writing the unprocessed raw data files to disk and subsequent transfer of the acquired data files (e.g., typically greater than 100 megabytes) to an off-line workstation.

As an example of comparing the invention with the conventional approach, Table 1 also includes the results from performing the same BOLD fMRI study, but using instead a

single DEC processor. Using the single processor, the computation time to process the large raw data BOLD fMRI files (i.e., 124 volumes of 64 x 64 by 36 slices) and produce t-maps was 15 minutes and 38 seconds. This included the time for disk retrieval of raw data using the single processor and the processing time using the software described above. In contrast, when all four processors on the computational server were used, the total processing time was 4 minutes and 29 seconds. Hence, using all four processors results in approximately a 3.5 fold increase in the speed of the data processing and analysis.

Table 2 summarizes the performance characteristics of the invention illustrated in Figure 3 used with the dynamic contrast fMRI study to calculate rCBV, TTP, and rCBF maps. The initial steps in the process are exactly the same as for the BOLD fMRI study, except that fewer whole brain volumes (80) are acquired over the 2 minutes and 40 seconds acquisition time. After completion of the MR data acquisition, it takes an additional 49 seconds using the invention to perform a voxel-by-voxel gamma variate fit of the time series data, search for the bolus TTP, determine the arterial input function used to calculate the rCBF maps, and display all three maps. Moreover, when the raw data dynamic contrast studies are processed from the disk using a single processor, the total processing time was 10 minutes and 8 seconds. Hence, with a single processor, a delay of 8 minutes and 8 seconds occurs, whereas with the invention, a delay of 49 seconds occurs.

TABLE 2
Performance Characteristics of System Configuration for Dynamic Contrast fMRI Examination

36 slice volume acquisition time:	2.0 sec/vol
Raw data volume size:	792000 bytes
DEC read volumes (processors 1, 2):	0.5 sec/vol
Reconstruction (processors 1, 2):	1.5 sec/vol
Registration (processors 3, 4):	1.5 sec/vol
Calculation of rCBV, rCBF, and TTP maps (processors 1-4):	29 sec.
Display of rCBV, rCBF, and TTP maps:	17 sec.
a) Total fMRI acquisition (80 volumes):	2 min. 40 sec.
b) Total processing time with dynamic contrast fMRI data acquisition:	3 min. 29 sec.
Processing time (b-a) after MR data collection ends:	49 seconds*
c) Total processing time with dynamic contrast fMRI data acquisition using a single DEC processor:	

	10 min. 8 sec.
Time ratio (c/b):	2.91

*includes delay time for the first volume to be completely acquired and transferred over the VME bus.

Using the invention, a BOLD fMRI exam was performed on a healthy control subject who was performing a sensorimotor activation by finger tapping at 2 Hz with the dominant hand. The data was processed using the invention illustrated in Figure 3. Figure 6 shows images produced by the invention for the finger tapping. In Figure 6, activated voxels in red are superimposed on top of axial spiral images for the five motor regions (i.e., primary sensorimotor, lateral premotor region, parietal region, supplementary motor area, and ipsilateral cerebellum) associated with right-handed finger tapping. With the invention, the images were obtained within 20 seconds after acquiring the raw image data from the BOLD fMRI exam using a threshold of 4.8.

With the invention, the normalized standard deviation histogram, along with a graph of patient motion which was obtained from the registration of the images, can be used as the criteria for rejecting a run or determining the necessity of repeating a given experimental run because of, for example, motion of the subject. In general, subject motion is difficult to address because, even when a registration finds the correct motion transformation, the ensuing interpolation reduces the high frequency components in the registered columns, which increases the standard deviation at each voxel position (32).

To illustrate this aspect of the invention, the BOLD fMRI examination was repeated three times during the fMRI exam session. In the first session, the subject was asked to remain motionless. In the second session, the subject was asked to move during the exam to simulate an uncooperative patient. In particular, the subject was asked to begin the session with the subject's head tilted to one side and then to rotate it slowly to the other side during the course of the experiment. To demonstrate the utility of the interactive nature of the invention, the subject was again asked to remain motionless, and a third BOLD fMRI data set was subsequently collected and analyzed.

Figure 5A shows the normalized standard deviation histograms from the three sequential studies. As can be seen, the histogram from the second BOLD fMRI exam has a wider distribution and is interpreted as an inadequate exam precluding any further analysis of the data set.

Figure 5B is a plot of the rotational motion correction applied by the COCGV registration for the three BOLD fMRI experiments. All subject motion is represented as a single rotation magnitude and a single translation magnitude. The axis of rotation and translation are not displayed.

Figure 7 shows rCBV, TTP, and rCBF maps produced by the invention for a dynamic contrast fMRI study. In Figure 7, each of the three rows shows six representative slices from a 36-slice whole brain dynamic contrast fMRI study performed on a healthy 25-year old male control volunteer following administration of 0.1 mm/kg Gadopentetate Dimeglumine as a bolus at 10 cc/sec. using an MR-compatible injector. Row A shows the resulting rCBV maps, row B shows the resulting rCBF maps, and row C shows the resulting TTP maps. These maps were produced from 80 whole brain spiral images and, with the invention, were displayed within 49 seconds after completion of the dynamic contrast study. Further, approximately 99% of the voxels were successfully fitted by the gamma variate function. These maps are consistent with results obtained from a healthy control subject.

The invention has been described in detail with respect to preferred embodiments, and it will now be apparent from the foregoing to those skilled in the art that changes and modifications may be made without departing from the invention in its broader aspects, and the invention, therefore, as defined in the appended claims is intended to cover all such changes and modifications as fall within the true spirit of the invention.

CLAIMS

What is claimed is:

1. A method for outputting examination results from a magnetic resonance image examination, comprising the steps of:

obtaining first and second acquisition volumes from a magnetic resonance image scanner during the magnetic resonance image examination;

processing the acquisition volumes from the magnetic resonance image scanner to obtain the examination results, comprising the sub-steps of:

reconstructing the first acquisition volume using a first processor to obtain a first reconstructed volume;

reconstructing the second acquisition volume using a second processor to obtain a second reconstructed volume; and

registering the second reconstructed volume using a third processor to obtain a second registered volume; and

outputting the examination results.

2. The method of claim 1, further comprising the steps of:

obtaining a third acquisition volume from the magnetic resonance image scanner during the magnetic resonance image examination; and

wherein processing acquisition volumes further comprises the sub-steps of:

reconstructing the third acquisition volume using the first processor to obtain a third reconstructed volume; and

registering the third reconstructed volume using a fourth processor to obtain a third registered volume.

3. The method of claim 2, further comprising the sub-steps of:

obtaining a fourth acquisition volume from the magnetic resonance image scanner during the magnetic resonance image examination; and

wherein processing acquisition volumes further comprises the sub-steps of:

reconstructing the fourth acquisition volume using the second processor to obtain a fourth reconstructed volume; and

registering the fourth reconstructed volume using the third processor to obtain a fourth registered volume.

4. The method of claim 1, further comprising the step of:

processing the examination results to obtain statistical results of the magnetic resonance image examination using a combination of the first, second, and third processors.

5. The method of claim 1, wherein the magnetic resonance image examination comprises one of a blood oxygenation level dependent (BOLD) based functional magnetic resonance imaging (fMRI) examination, a dynamic contrast fMRI examination, a profusion imaging fMRI examination, a cardiac fMRI examination, diffusion imaging examination, and a spectroscopic imaging examination.

6. The method of claim 1, wherein outputting the examination results comprises at least one of displaying the examination results, saving the examination results to a computer-readable medium, transferring the examination results over a network, and printing the examination results.

7. The method of claim 1, wherein the examination results comprise at least one of a magnetic resonance image, an activation map, a relative cerebral blood volume (rCBV) map, a relative cerebral blood flow (rCBF) map, a time-to-peak (TTP) map, an activation s-map, an activation t-map, and an activation error histogram.

8. A method for outputting examination results from a magnetic resonance image examination, comprising the steps of:

obtaining first and second acquisition volumes from a magnetic resonance image scanner during the magnetic resonance image examination;

processing the acquisition volumes from the magnetic resonance image scanner to obtain the examination results, comprising the sub-steps of:

reconstructing the first acquisition volume using a first processor to obtain a first reconstructed volume;

reconstructing the second acquisition volume using the first processor to obtain a second reconstructed volume; and

registering the second reconstructed volume using a second processor to obtain a second registered volume; and

outputting the examination results.

9. An apparatus for outputting examination results from a magnetic resonance image examination, comprising:

means for obtaining first and second acquisition volumes from a magnetic resonance image scanner during the magnetic resonance image examination;

means for processing the acquisition volumes from the magnetic resonance image scanner to obtain the examination results, comprising:

means for reconstructing the first acquisition volume using a first processor to obtain a first reconstructed volume;

means for reconstructing the second acquisition volume using a second processor to obtain a second reconstructed volume; and

means for registering the second reconstructed volume using a third processor to obtain a second registered volume; and

means for outputting the examination results.

10. An apparatus for processing data from a magnetic resonance image examination, comprising:

a magnetic resonance image scanner for producing a plurality of acquisition volumes obtained during the magnetic resonance image examination;

at least one first processor for reconstructing the plurality of acquisition volumes to obtain a plurality of reconstructed volumes; and

at least one second processor for registering the plurality of reconstructed volumes to obtain a plurality of registered volumes.

11. The apparatus of claim 10, further comprising:

means for processing the plurality of registered volumes to obtain statistical information; and

means for outputting the statistical information.

12. A computer-readable medium embodying code segments for a magnetic resonance image examination, the code segments comprising:

code segments for controlling the magnetic resonance image examination to obtain a plurality of acquisition volumes;

code segments for controlling at least one first processor to reconstruct the plurality of acquisition volumes to obtain a plurality of reconstructed volumes; and

code segments for controlling at least one second processor to register the plurality of reconstructed volumes to obtain a plurality of registered volumes.

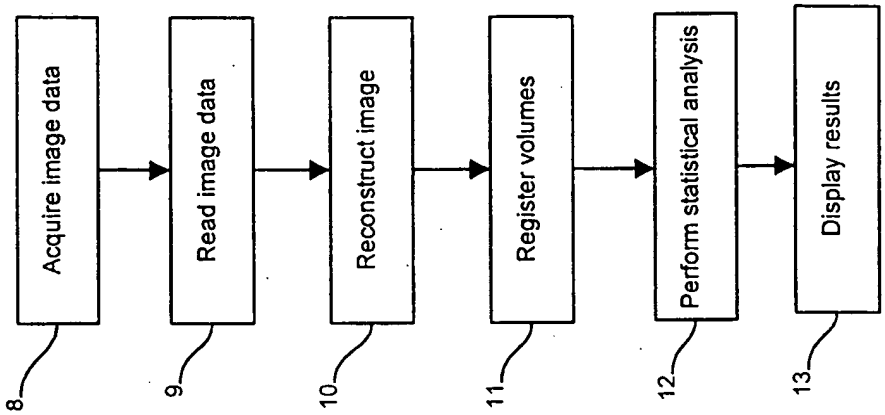


Figure 2

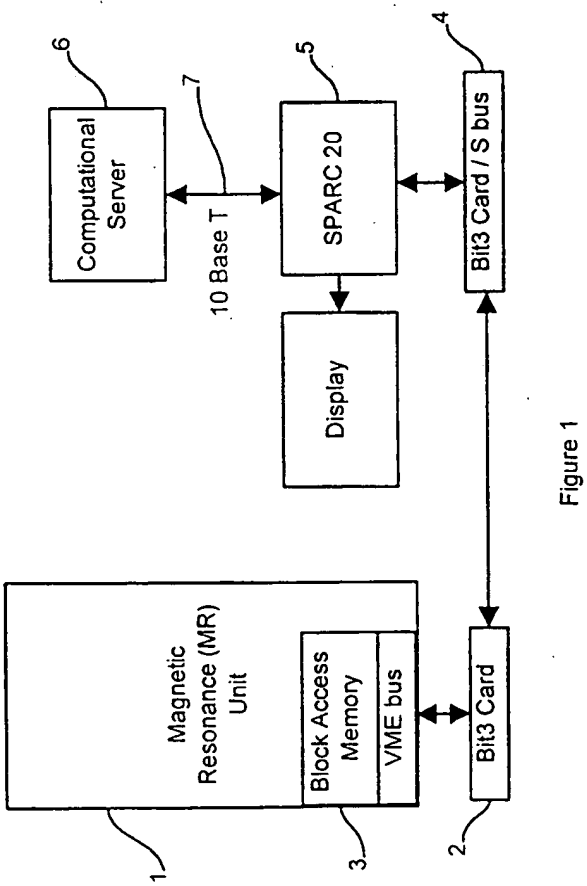


Figure 1

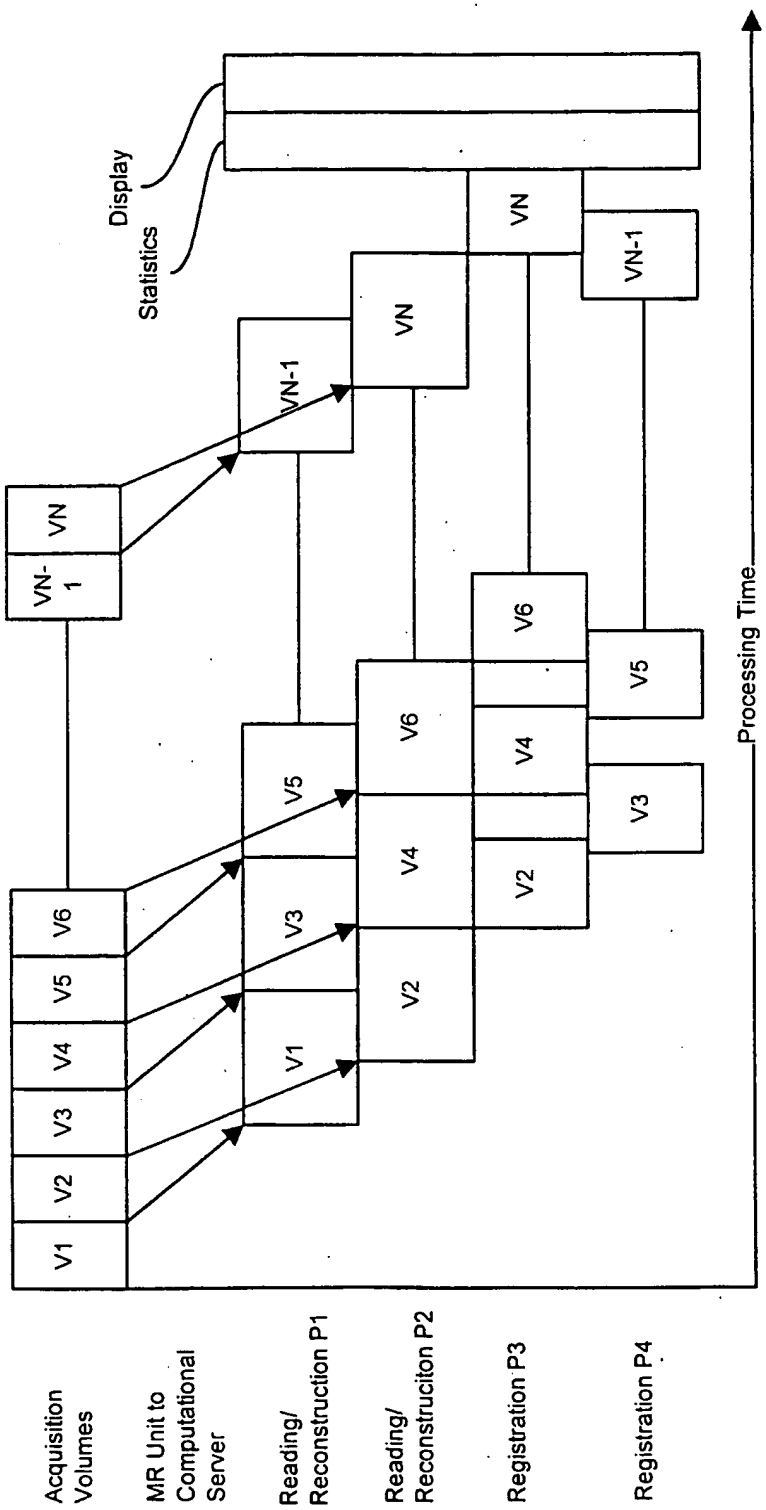

Display
Statistics
VN
VN-1
VN
VN-1
V6
V5
V4
V3
V2
V1
Processing Time
Acquisition Volumes
MR Unit to Computational Server
Reading/ Reconstruction P1
Reading/ Reconstruciton P2
Registration P3
Registration P4

Figure 3

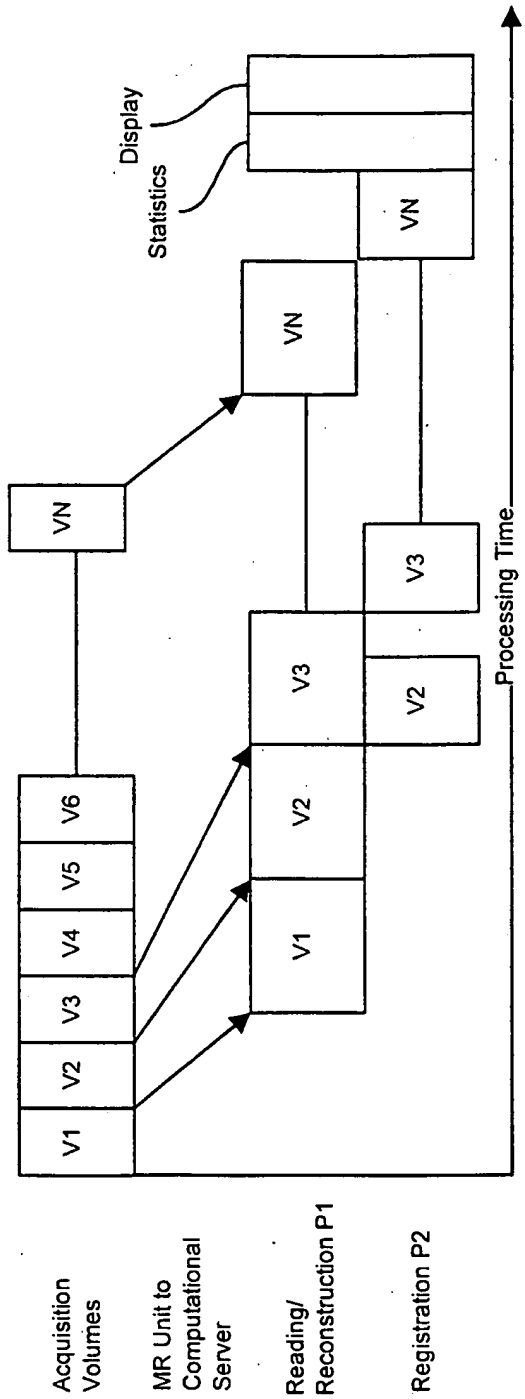

Display
Statistics
VN
VN
VN
V3
V3
V2
V2
V1
V6
V5
V4
V3
V2
V1
Processing Time
Acquisition Volumes
MR Unit to Computational Server
Reading/ Reconstruction P1
Registration P2

Figure 4

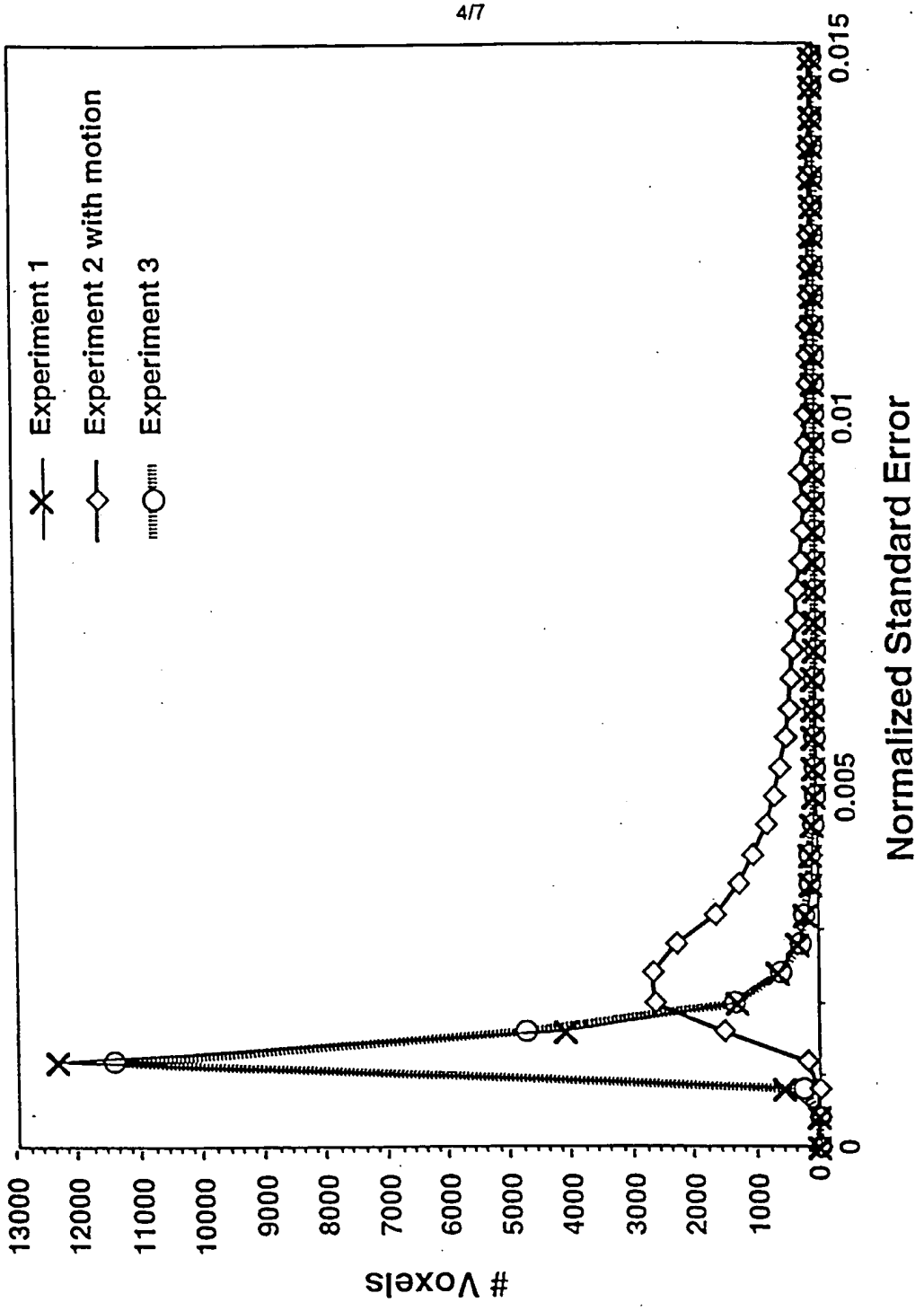

Experiment 1
Experiment 2 with motion
Experiment 3
Voxels
Normalized Standard Error
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
0.005
0.01
0.015

Figure 5A

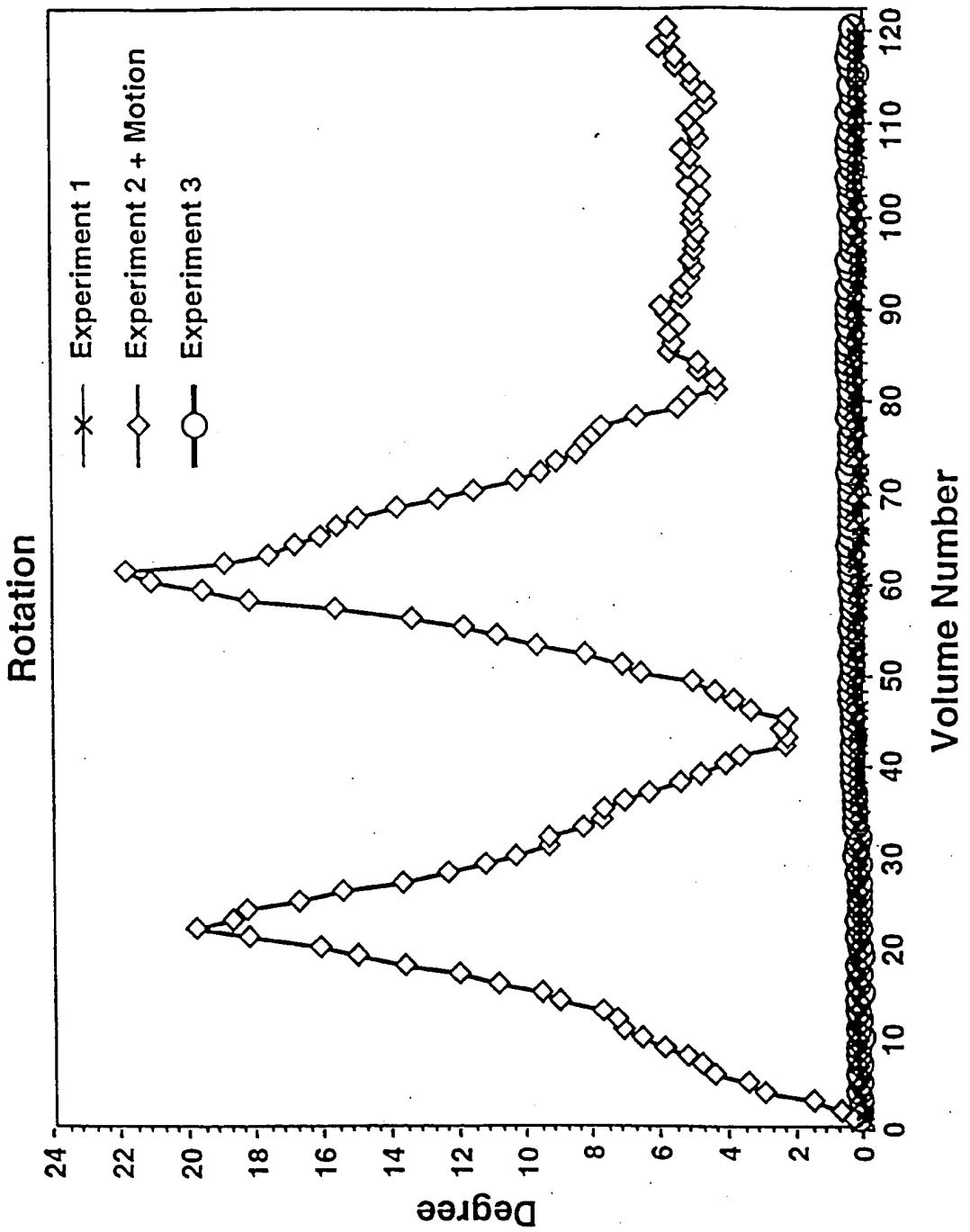

Rotation
Experiment 1
Experiment 2 + Motion
Experiment 3
Degree
Volume Number
0
2
4
6
8
10
12
14
16
18
20
22
24
0
10
20
30
40
50
60
70
80
90
100
110
120

Figure 5B

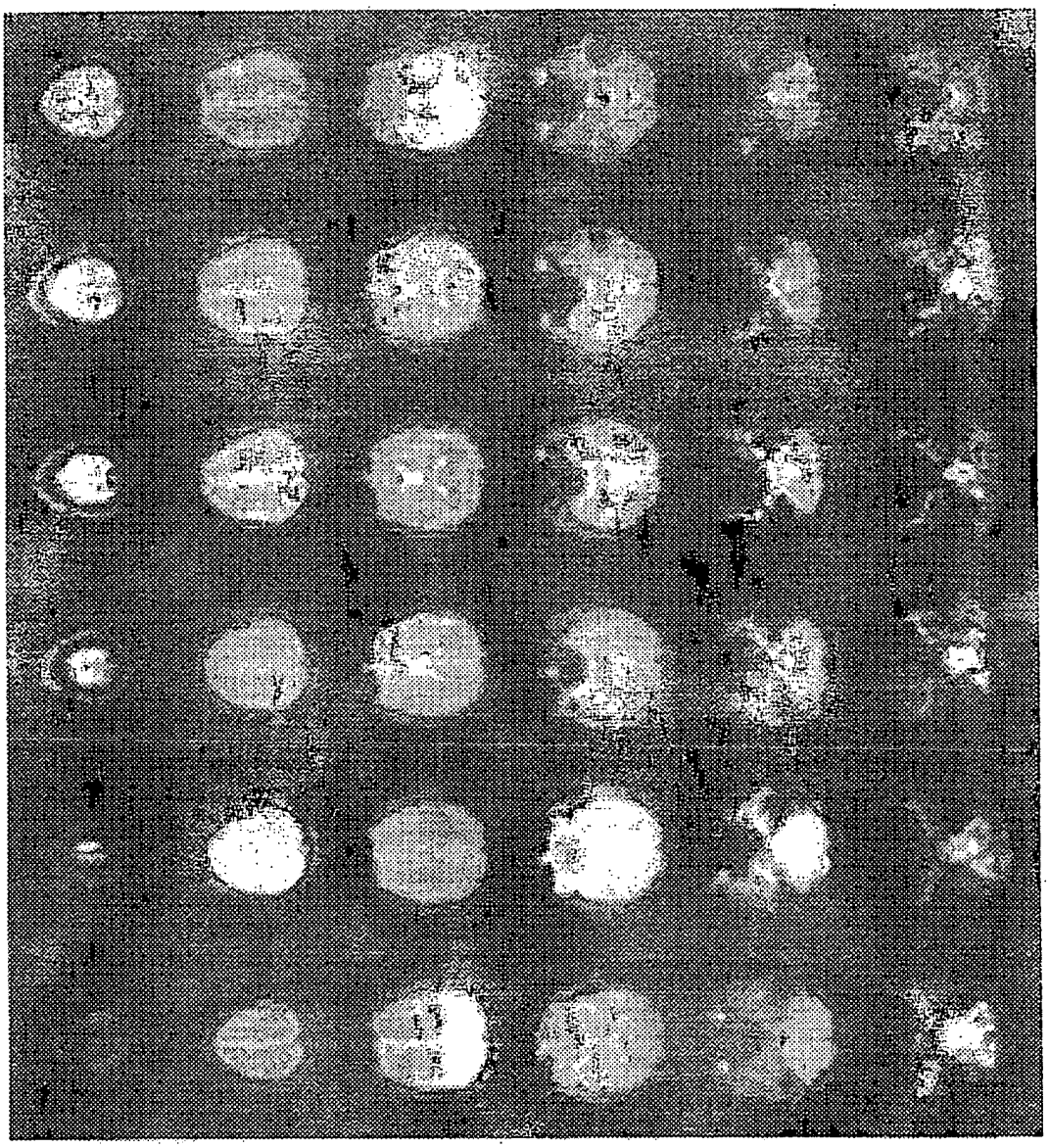


Figure 6

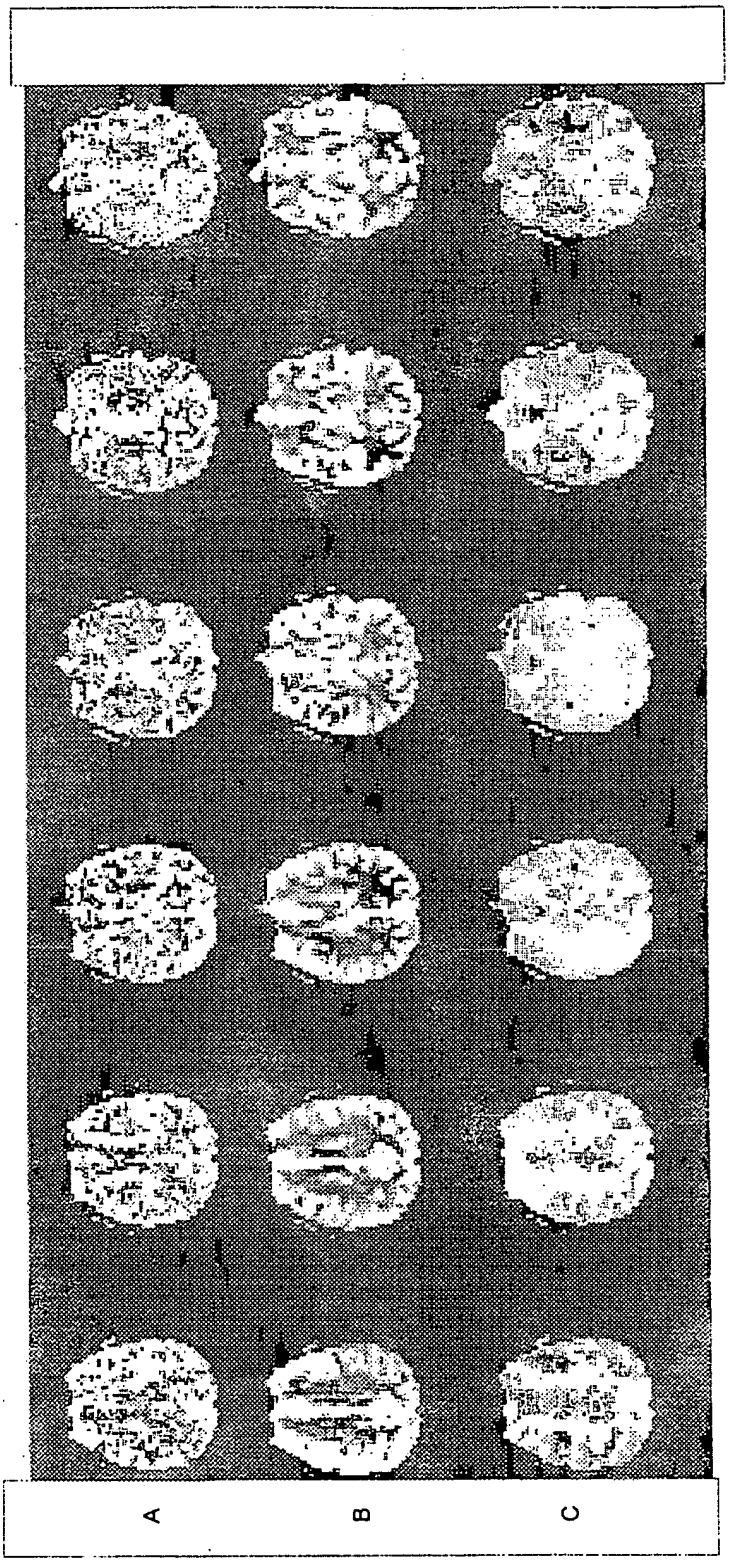


Figure 7

INTERNATIONAL SEARCH REPORT

Inter' 'onal Application No
PC1/US 99/12443

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01R33/54

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01R

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category '	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GODDARD N H ET AL: "ONLINE ANALYSIS OF FUNCTIONAL MRI DATASETS ON PARALLEL PLATFORMS" JOURNAL OF SUPERCOMPUTING, vol. 11, no. 3, 1 January 1997 (1997-01-01), pages 295-318, XP000724662 ISSN: 0920-8542 see the whole document	1-12
A	KERR A B ET AL: "REAL-TIME INTERACTIVE MRI ON A CONVENTIONAL SCANNER" MAGNETIC RESONANCE IN MEDICINE, vol. 38, no. 3, 1 September 1997 (1997-09-01), pages 355-367, XP000699718 ISSN: 0740-3194 cited in the application	1-12

☐ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

' Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 September 1999	28/09/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lersch, W

Form PCT/ISA/210 (second sheet) (July 1992)